

2

Docket No. G-085US04CON
Serial No. 09/818,260In the Claims

1. (Currently Amended) A method of determining the statistical significance of a difference between haplotype frequency of a least two groups of individuals comprising:

a) obtaining and assigning haplotypes to all individuals in one of said at least two groups of individuals;

b) obtaining and assigning haplotypes to all individuals in another of said at least two groups of individuals;

c) identifying the haplotypes of all individuals in each of said at least two groups with a binary code;

d) analyzing the haplotypes of said at least two groups of individuals comprising the steps of:

determining the combined likelihood that said at least two groups of individuals are derived from the same distribution of haplotypes;

determining the sum of the separate likelihoods that each of said at least two groups of individuals are derived from the same distribution of haplotypes;

determining the difference of said sum and said combined likelihood; and

determining the significance of this difference by simulating hypothetical groups by randomly permuting the haplotypes between groups to determine the probability that the groups do not come from the same distribution of haplotypes.

2-3. (Canceled)

4. (Currently Amended) A system for determining the statistical significance of the difference between haplotype frequency profiles of at least two groups of individuals, comprising:

first instructions that assign a binary code to the haplotype of each individual of said at least two groups of individuals;

3

Docket No. G-085US04CON
Serial No. 09/818,260

~~first~~second instructions for determining the combined likelihood that said at least two groups of individuals are derived from the same distribution of haplotypes;

~~second~~third instructions for determining the sum of the separate likelihoods that each of said at least two groups of individuals are derived from the same distribution of haplotypes;

~~third~~fourth instructions for determining the difference of said sum and said combined likelihood; and

~~fourth~~ fifth instructions for determining the significance of this difference by simulating hypothetical groups by randomly permuting the haplotypes between groups to determine the probability that the groups do not come from the same distribution of haplotypes;

wherein said system comprises a programmed storage device comprising at least one module or one or more computer.

5-6. (Canceled)

7. (Currently Amended) A programmed storage device comprising instructions that when executed perform a method comprising:

assigning a binary code to the haplotype of each individual of said at least two groups of individuals;

determining the statistical significance of the difference between haplotype frequency profiles of at least two groups of individuals by comprising comparing the final likelihood that all groups of individuals come from the same distribution of haplotypes with the sum of the final likelihoods for each group separately; and

determining the significance of this difference by simulating hypothetical groups by randomly permuting the haplotypes between groups to determine the probability that the groups do not come from the same distribution of haplotypes.

8-39. (Canceled)

40. (New) A method of determining the statistical significance of a difference between haplotype frequency of a least two groups of individuals comprising:

a) obtaining and assigning haplotypes to all individuals in one of said at least two groups of individuals;

b) obtaining and assigning haplotypes to all individuals in another of said at least two groups of individuals;

c) identifying the haplotypes of all individuals in each of said at least two groups with a binary code;

d) analyzing the haplotypes of said at least two groups of individuals comprising the steps of:

determining the combined likelihood that said at least two groups of individuals are derived from the same distribution of haplotypes;

determining the sum of the separate likelihoods that each of said at least two groups of individuals are derived from the same distribution of haplotypes;

determining the difference of said sum and said combined likelihood; and

determining the statistical significance of the difference of said sum and said combined likelihood by simulating hypothetical groups by randomly permuting the haplotypes between groups to determine the probability that the groups do not come from the same distribution of haplotypes; and

e) further comprising the step of calculating all possible single-haplotype chi-square tests in order to provide measures of association between groups for a particular haplotype.

41. (New) A method of determining the statistical significance of a difference between haplotype frequency of a least two groups of individuals comprising:

a) obtaining and assigning haplotypes to all individuals in one of said at least two groups of individuals;

b) obtaining and assigning haplotypes to all individuals in another of said at least two groups of individuals;

5

Docket No. G-085US04CON
Serial No. 09/818,260

c) identifying the haplotypes of all individuals in each of said at least two groups with a binary code;

d) analyzing the haplotypes of said at least two groups of individuals comprising the steps of:

determining the combined likelihood that said at least two groups of individuals are derived from the same distribution of haplotypes;

determining the sum of the separate likelihoods that each of said at least two groups of individuals are derived from the same distribution of haplotypes;

determining the difference of said sum and said combined likelihood; and

determining the statistical significance of the difference of said sum and said combined likelihood by simulating hypothetical groups by randomly permuting the haplotypes between groups to determine the probability that the groups do not come from the same distribution of haplotypes; and

e) further comprising assessing the statistical significance of individual haplotypes using an odds ratio or a P-excess value in order to provide measures of association between groups for a particular haplotype.

42. (New) The method according to claim 41, further comprising drawing an inference from any statistical significance in the differences of haplotype frequency of said at least two groups of individuals.

43. (New) The system according to claim 4, wherein said system comprises at least one computer.

44. (New) The system according to claim 4, wherein said system comprises an electronically connected group of computers.

45. (New) The system according to claim 4, wherein said system comprises a programmed storage device comprising at least one module.

J:\GIN\085.US04.CON\Amend-Resp\Amd.doc\1\NH/st

46. (New) A system for determining the statistical significance of the difference between haplotype frequency profiles of at least two groups of individuals, comprising:

first instructions that assign a binary code to the haplotype of each individual of said at least two groups of individuals;

second instructions for determining the combined likelihood that said at least two groups of individuals are derived from the same distribution of haplotypes;

third instructions for determining the sum of the separate likelihoods that each of said at least two groups of individuals are derived from the same distribution of haplotypes;

fourth instructions for determining the difference of said sum and said combined likelihood;
and

fifth instructions for determining the significance of this difference by simulating hypothetical groups by randomly permuting the haplotypes between groups to determine the probability that the groups do not come from the same distribution of haplotypes; and

sixth instructions for calculating all possible single-haplotype chi-square tests in order to provide measures of association between groups for a particular haplotype;

wherein said system comprises a programmed storage device comprising at least one module or one or more computer.

47. (New) A system for determining the statistical significance of the difference between haplotype frequency profiles of at least two groups of individuals, comprising:

first instructions that assign a binary code to the haplotype of each individual of said at least two groups of individuals;

second instructions for determining the combined likelihood that said at least two groups of individuals are derived from the same distribution of haplotypes;

third instructions for determining the sum of the separate likelihoods that each of said at least two groups of individuals are derived from the same distribution of haplotypes;

fourth instructions for determining the difference of said sum and said combined likelihood;
and

fifth instructions for determining the significance of this difference by simulating hypothetical groups by randomly permuting the haplotypes between groups to determine the probability that the groups do not come from the same distribution of haplotypes; and

sixth instructions for calculating the statistical significance of individual haplotypes using an odds ratio or a P-excess value in order to provide measures of association between groups for a particular haplotype;

wherein said system comprises a programmed storage device comprising at least one module or one or more computer.

48. (New) A programmed storage device comprising instructions that when executed perform a method comprising:

assigning a binary code to the haplotype of each individual of said at least two groups of individuals;

determining the statistical significance of the difference between haplotype frequency profiles of at least two groups of individuals by comprising comparing the final likelihood that all groups of individuals come from the same distribution of haplotypes with the sum of the final likelihoods for each group separately;

determining the significance of this difference by simulating hypothetical groups by randomly permuting the haplotypes between groups to determine the probability that the groups do not come from the same distribution of haplotypes; and

calculating the statistical significance of individual haplotypes using an odds ratio or a P-excess value in order to provide measures of association between groups for a particular haplotype.

49. (New) A programmed storage device comprising instructions that when executed perform a method comprising:

assigning a binary code to the haplotype of each individual of said at least two groups of individuals;

determining the statistical significance of the difference between haplotype frequency profiles of at least two groups of individuals by comprising comparing the final likelihood that all groups of

individuals come from the same distribution of haplotypes with the sum of the final likelihoods for each group separately;

determining the significance of this difference by simulating hypothetical groups by randomly permuting the haplotypes between groups to determine the probability that the groups do not come from the same distribution of haplotypes; and

calculating all possible single-haplotype chi-square tests in order to provide measures of association between groups for a particular haplotype.

50. (New) A method of determining the statistical significance of a difference between haplotype frequency of a least two groups of individuals comprising:

- a) obtaining and assigning haplotypes to all individuals in one of said at least two groups of individuals and coding said haplotypes with binary mask arrays;
- b) obtaining and assigning haplotypes to all individuals in another of said at least two groups of individuals and coding said haplotypes with binary mask arrays;
- d) analyzing the haplotypes of said at least two groups of individuals comprising the steps of:
 - 1) determining the combined likelihood that said at least two groups of individuals are derived from the same distribution of haplotypes;
 - 2) determining the sum of the separate likelihoods that each of said at least two groups of individuals are derived from the same distribution of haplotypes;
 - 3) determining the difference of said sum and said combined likelihood; and
 - 4) determining the significance of this difference by simulating hypothetical groups by randomly permuting the haplotypes between groups to determine the probability that the groups do not come from the same distribution of haplotypes.